REMARKS/ARGUMENTS

The above-identified application has been amended without prejudice in that claims 34, 36 and 46 have been amended.

Examiners Richter and Gollamudi are thanked for the courtesy of the telephone interview of April 9, 1007. Where appropriate, the interview will be referred to in the following Remarks.

Claims 15, 16, 18-25, 30, 31, 33, 34, 36 and 39-50 have been rejected under 35 U.S.C. §112, second paragraph, as indefinite. It is submitted that this rejection is improper and should be withdrawn.

Claims 34 and 36 have been reorganized in that subsections (i)-(iii) under (a) of claims 34 and 36 have been delineated. This amendment should address the question raised by the Examiner on pages 2 and 3 of the Official Action as whether the "alkaline reacting compound" is part of the Markush group identifying the active ingredients. Also see the specification at pages 12 and 13. The claims also have been amended to indicate that the active ingredient consists of a compound with anti-ulcer activity in accordance with the formulae recited therein.

The invention defined by the now pending claims is for a process of producing a pharmaceutical preparation of an active ingredient which is a proton pump inhibitor and of the class of compounds known as substituted benzimidazoles. Such compounds are known to be particularly acid labile and to degrade rapidly when exposed to an acidic environment. See Lovgren's U.S. Patent No. 4,853,230 ("the '230 Patent") discussing the acid sensitivity of this class of compounds. When such compounds are exposed to the gastric environment, they can degrade within the stomach. This is not desirable. A

common approach to protecting dosage forms is to use an enteric coating. However, enteric coatings are also somewhat acidic and thus can cause premature degradation of the highly acid sensitive benzimidazole proton pump inhibitors. Lovgren proposed using a separating layer to separate the active ingredient and alkaline material from the enteric coating. See Lovgren's U.S. Patent No. 4,786,505 ("the '505 Patent") and the '230 Patent. This approach is used in the Prilosec® dosage form of omeprazole currently marketed in the U.S.

THE OBVIOUSNESS REJECTIONS

Claims 15, 16, 18 to 25, 30, 31, 33, 34, 36, 39 to 50 were rejected under 35 U.S.C. §103(a) as unpatentable over U.S. Patent No. 6,365,184 to Depui et al. ("Depui '184") alone or in view of U.S. Patent No. 2,799,241 to Wurster. It is submitted the rejection is improper and should be withdrawn.

The disclosure of the '184 patent, which is largely duplicative of the disclosure in Depui '771, has been discussed extensively in prior responses and those comments are incorporated by reference as if set forth here at length. Neither of Depui '184 or Depui '771 are focused on process technology and what information is provided regarding the process or processes used in those references is at best superficial.

With respect to process considerations, it appears the Examiner's only comment different from Depui '771 is in reference to example 4 of Depui '184. However, neither that example nor any other disclosure in Depui '184 suggests the now claimed subject matter.

Presumably, the Examiner considers example 4 to present her best case based on this reference. However, the reference does not suggest the now claimed subject matter.

It is clear from the wording of example 4 that there are at least two separate operational apparatus employed, and the example is directed to providing a multi-active containing tablet. Further, it is also clear that in example 4 there is a separating layer applied on to the suspension layered core. Subsequently, an enteric coating is applied on the separating layer. This is in direct contrast to the present claim language wherein the enteric coating solution is sprayed to form a gastro-resistant external coating layer on the charged nucleus. Depui '184 fails to suggest that the nucleus is formed with a substantially non-porous active containing layer as is clearly recited in the presently pending claims.

The Office Action does not dispute that example 4 contains a separating layer nor does the Office Action dispute that there is no example of a dosage form without a separating layer. The Office Action does not dispute the failure of not only the example, but the entire reference, to suggest the seed is coated with a substantially non-porous active containing layer. Thus, no conclusion of obviousness is justified.

It is clear from the disclosure of Depui '184 that the problems which that reference seeks to address in both the product and process for making that product are those which arise in a single fixed unit dosage form containing multiple active substances that have different physical, chemical and pharmacological properties. According to the reference, preparation of multiple unit dosage forms give rise to specific problems not encountered in a single active dosage form. See col. 2, ll. 52 to 63.

Depui '184 does not show, suggest, or enable an embodiment of the dosage form utilizing a proton pump inhibitor compound wherein the enteric coating layer is deposited directly on the charged nucleus without an intermediate separating layer.

The Examiner refers to column 10, lines 41 to 43, and maintains that the reference discloses "the optionally applied separating layer is not essential for the invention". However ,such phraseology does not amount to a disclosure of how to make such an embodiment.

Applicant has made a of record substantial evidence traversing the rejections but that evidence has not been properly considered.

As discussed with the Examiners during the interview of April 9, 2007, the Lovgren '505[1] patent, which is acknowledged in the Depui reference in column 2, lines 47 to 50, is evidence showing that in the prior art a proton pump inhibitor dosage form without a separating layer, resulted in a dosage form which was not stable. During the interview, the Examiners' attention was invited to Tables 1 to 3 of Lovgren '505. Table 1 of the '505 Patent shows core compositions 1-7 and Table 2 shows formulations I-IV for coatings for separating layers and enteric coatings for those core compositions. However, the I formulations do not contain an inner or outer separating layer but do contain an enteric coating layer. Table 3 shows the stability of each of the formulations as a function of the different coating techniques which are listed left-hand most of the Table 3, i.e. Roman numerals I through IV. All of the core compositions 1 through 7, which were not coated with a separating layer before application of the enteric coating, showed some degree of deterioration within seven days. In that 7 day period, some of the compositions showed a substantial degree of deterioration starting as white but turning brown. Even the core materials that were treated with a coating formulation in accordance with Roman numeral II, in some instances, also showed signs of deterioration within seven days while many of those that did have the inner and outer separating layers separating the core from the

[1] Lovgren '505 and '230 have a common assignee with the Depui '184 and '771 Patents.

enteric coating showed little or no deterioration. Since Depui '184 specifically references the Lovgren '505 patent, one of ordinary skill would have expected Depui '184 to contain disclosure as to how to make a stable dosage form without a separating layer and provide an enabling disclosure as to that embodiment if the patentee had any knowledge as to how to do so. However, the best that has been offered in any of the Office Actions with respect to either Depui '184 or '771 is that they refer to the use of the separating layer as an option.

It is submitted that where the art was aware that a separating layer was needed, the Depui '184 statement that a separating layer is not essential cannot be considered as providing an enabling disclosure or realistic suggestion since the remainder of the reference provides absolutely no discussion or disclosure as to how to proceed to make a stable dosage form without the separating layer. As earlier indicated, there is not one single example in the patent relating to the dosage forms that teach how to proceed without a separating layer to obtain at a stable dosage form. Depui '184 at best shows obviousness to try, not obviousness. However, Lovgren '505 and '230 dispels any reasonable expectation of success. Accordingly, neither of Depui '184 or '771 can be elevated to show or suggest anything more than obviousness to try.

As discussed with the Examiners during the April 9, 2007 telephone interview, Applicant has a number of times raised the issue that the '505 Patent teaches contrary to what the Depui '771 or '184 patent is being interpreted as disclosing or suggesting. However, the PTO's position has been that since the rejection was not founded on Lovgren '505 that patent need not be considered or addressed[2]. As indicated during the telephone interview of April 9, 2007, this is in direct contradiction to *In re Piasecki*, 223

[2] This also validates 35 U.S.C. 103 requiring the art be considered as a whole.

USPQ 785, 788 (Fed. Cir. 1984). *Piasecki* is specifically referred to in MPEP 716.01(d) as containing a detailed discussion of the proper roles of an Examiners' *prima facie* case[3] and applicant's rebuttal evidence in the final determination of obviousness. In *Piasecki*, the court cited to *In re Rinehart*:

> When prima facie obviousness is established and evidence is submitted in rebuttal, the decision-maker must start over.*** An earlier decision should not, as it was here, be considered as set in concrete, and applicant's rebuttal evidence then be evaluated only on its knockdown ability. Analytical fixation on an earlier decision can tend to provide that decision with an undeservedly broadened umbrella effect. Prima facie obviousness is a legal conclusion, not a fact. Facts established by rebuttal evidence must be evaluated along with the facts on which the earlier conclusion was reached, not against the conclusion itself.***[A] final finding of obviousness may of course be reached, but such finding will rest upon evaluation of all facts in evidence, uninfluenced by any earlier conclusion reached by an earlier board upon a different record.

In the present matter, Lovgren '505, Lovgren '230, the Molina declaration, the Johansson declaration and the Molina-Millián declaration have not been accorded the proper weight in accordance with *Piasecki* or *Rinehart*. That is, the disclosures of Depui '184 or Depui '771 have not be evaluated in light of any of Applicant's submitted evidence but have been considered as set in stone while contrary evidence or art has been deflected or ignored.

Depui, starting in col. 13, at about line 36, discusses her process for manufacture of the dosage forms discussed therein. In particular, Depui at col. 13, ll. 36 to 46, states as follows:

> The process for the manufacture of the dosage form represents a further aspect of the invention. After formulation of the pellets by spraying coating or layering of the proton pump inhibitor onto seeds, or by

[3] Applicant herein disputes that the Examiner has established a *prima facie* case.

> extrusion/sphernization or granulation, e.g. rotor granulation of homogeneous pellets, the pellets are first optionally covered with the separating layer(s) and then with the enteric coating layer(s) or a separating layer spontaneously developed in situ between the alkaline core material and the enteric coating material. The coating is carried out as described above and in the accompanying examples. (Underling added)

There is not a single mention in this paragraph of a fluidized bed in connection with applying the active ingredient coating or the enteric coating. What is specifically mentioned is rotor granulation or extrusion/sphernization. Clearly, the reference does not recognize or teach any preference as to how to apply the layer. Clearly, the reference does not recognize or suggest a substantially non-porous active containing layer. As already established by the Molina Declaration, the use of rotor granulation produces an inferior and unacceptable product.

The presently pending claims clearly recite the presence of an alkaline reacting compound in the aqueous or hydroalcoholic suspension-solution which also contains the active ingredient. As established by the Johansson Declaration, repetition of example 5 of the Depui '771 but without the separating layer results in an inferior product showing immediate degradation as is indicated by the brown color[4]. Thus, the Examiner's previous position that one could simply follow the Depui '771 examples but omit the separating layer has been shown to be in error. There is no reason set forth in the prior art to expect the results would be any different with any example in either of Depui '771 or '184.

The Office Action asserts that Wurster teaches that a Wurster-type fluidized apparatus provides a uniform coating preventing a coating material from sticking to the inner surface of the chamber.

[4] In contrast, products made by the now claimed process have been approved by the regulatory authority of at least one European country which indicates the product has a suitable stability and product life.

Applicants do not deny that a Wurster-type fluidized apparatus was known. However, what is not disclosed or suggested in any of the references is that by utilizing this type of apparatus, one can obtain a substantially non-porous homogeneous soluble active layer which can eliminate the need for a separating layer in those types of formulations where the prior art required the presence of the separating layer to protect the active ingredient from the deleterious affects of enteric coatings. None of the cited art provides a disclosure or suggestion of such a feature or how to obtain it. See *Ex parte Wisdom & Hilton*, 184 USPQ 822, 823 (POBA 1973) (process claim not obvious based on reference which doesn't recognize problem solved by Applicant).

Further, the combination of references is not motivated by the art but is clearly the product of hindsight reconstruction. There is no *prima facie* case of obviousness and the rejection is improper.

In responding to the previously submitted arguments the Examiner has relied on certain arguments and repeats them in response to each of Applicant's traverse of each of the previous anticipation and obviousness rejections. In the interest of not burdening the file with further repetition, Applicant will set forth its position as the Examiner's response only once unless necessary. It should be understood that Applicant's comments apply to each instance where the Examiner has made the same response.

The Term Comprising

The Examiner states that because claims 34 and 36 recite "comprising language" it is not exclusionary. However, the wording of the claims clearly indicate a separating layer is excluded. During the telephone interview of April 9, 2007, Applicant raised this issue. The Examiner stated that she raised this issue because of Applicant's argument regarding

the number of active ingredients in the Depui dosage form in contrast to the language of the present claims. However, it is clear from the discussion bridging pages 8 and 9 of the specification that the definition of "comprising" is being used to alter or unreasonably interpret the limitations expressly stated in the claims. The record does not contain any case authority or any section of the MPEP which permits the PTO to alter a limitation, or interpret it in a manner inconsistent with the specification, because of the use of the transitional phrase "comprising".

Claim Construction

Also, it is clear from the Office Action citations that the Examiner is engaging in claim construction. For purposes of examination, the Examiner is only permitted to interpret the claims as broadly as is reasonably supported by the specification. There is no mention in the specification of a second active ingredient being present. Thus, the Examiner has engaged in an interpretation of a claim beyond that which is permitted. Further, neither *PPG* nor *AK Steel Corp.* have any relevance to the present issues. Both cases involved an extensive analysis of the specification of each of the patents there at issue as well as extrinsic evidence. The Examiner has not set forth any such analysis here. Claims 34 and 36 have been amended to indicate that the only active is an anti-ulcer compound.

The Word "Optional"

Applicant takes issue with the Examiner's conclusion that because the reference uses the word "optional" it is implicit that the formulation can function stably without the separating layer. This is not the scientific fact nor is it a justifiable inference from the disclosure. Further, reliance on dictionary definitions is not favored. See *Phillips v. AWH*

Corp., 75 USPQ 2d 1321 (Fed. Cir. 2005). The Examiner is attempting to apply "inherency" in the context of a Section 103 rejection. This is contrary to the law.

In re Petering does not apply. *Petering* did not involve an issue of enablement where the prior art was shown to lack enablement as to the cited subject matter of the reference. If the proper standard of reconsideration as enunciated in *Piasecki* is applied and any of Lovgren '505, Lovgren '230, or any of the declarations is properly considered, if is clear that there is not a legally sufficient case of obviousness. Nor is there a *prima facie* case. See *In re Benno*, 226 USPQ 603,688 (where there is no mention of the problem to be solved there is no *prima facie* case to overcome by the submission of evidence).

The Declarations

At page 18, the Office Action appears to either confuse or improperly intermingle the concept of showing "unexpectedness" (which presumably is a shorthand reference to unexpected results or benefits) and enablement. While certainly enablement is required for a reference to anticipate, the Examiner cannot dismiss or fail to address the merits of a 132 Declaration that shows unexpected benefits by relegating the showing only to enablement when there is an obviousness rejection relying in part on the same reference previously used for an anticipation rejection. Nor can the Examiner dismiss the declaration which shows lack of enablement of the prior art by referring to issues regarding unexpected results.

Applicant repeats the declarations that have been submitted herein such as the Molina declaration, the Johansson declaration and the most recent Molina-Millián declaration have not been addressed. It is clear from the Office Action that the

declarations have been given no weight for reasons which are either not relevant or based on information not of record.

The Office Actions continue to ignore the fact that the cited prior art does not provide process details to enable one to repeat any of the examples therein. As such, Applicant has been placed in a position having to attempt clairvoyance or make comparisons with closer or cumulative prior art which provides operational detail,. Applicant has repeatedly cited *In re Fouche* for the proposition, which is also cited in the MPEP, but the Office Actions continue to ignore this principle and fails to address the issue.

The Molina Declaration

The previously submitted Declaration by Dr. Molina, Mr. Picornell and Mr. Bravo ("the Molina Declaration") sets forth the attempts to reproduce Example 6 of Takeda '797. This experimental work led to the following conclusion:

> *"Therefore, even after correcting the defect of the procedure described in section 1) of example 6 of European Patent Application EP 0 642 797 in relation to the quantity of binder material, this procedure does not yield enteric-coated gastroresistant granules of lansoprazole that are appropriate and acceptable from the pharmaceutical standpoint. Consequently, the use of the above procedure does not yield granules equal or similar to those obtained with the procedure contemplated in Patent Application PCT WO 99/06032, particularly as described in example 1 therein."*

Therefore, when enteric-coated gastroresistant benzimidazole granules are made by powder-layering technique using a centrifugal fluidized coating granulator without a separating layer between the active layer and the enteric coating, it results in granules having stability problems and unacceptable low resistance to gastric fluid. See Paragraph No. 5 of that declaration.

The Johansson Declaration

The previously submitted Johansson declaration used Depui's '771 example 5 but omitted applying the separating layer. The omission of the separating layer resulted in dosage forms which showed rapid (within one hour) degradation of the active ingredient. This rapid degradation was not unexpected because such degradation was foretold by the prior art, specifically Lovgren '505 discussed above. In contrast, the present specification shows that the now claimed products produced by the now claimed process have stability over extended periods. The Examiner is again invited to look at the examples of the invention in the originally filed specification.

The Molina-Millián Declaration

In the most recently submitted declaration, Dr. Molina-Millián reports on another comparative test. In this test, the declarant fairly reproduced the first step of Example 11 of WO '624 to obtain enteric coated pellets prior to those pellets being compressed to form tablets. The details of the procedure are set forth in that declaration. The declarant produced enteric coated pellets of lansoprazole and pantoprazole, both of which are substituted benzimidazoles proton pump inhibitors currently on the market in the U.S. As noted in Paragraph 10 of the declaration, in each instance, a core material with a creamy white color was obtained prior to the application of the enteric coating.

Annex 1 attached to that declaration shows, in Figure 1, enteric coated lansoprazole pellets and, in Figure 2, enteric coated pantoprazole pellets each according to Example 11 of WO '624. Figure 3 shows lansoprazole pellets according to Example 1 of the present application. As can be observed from Figures 1 and 2, those pellets produced

according to Example 11 of WO '624 rapidly underwent a color change signifying degradation, or lack of stability, of the active ingredient in the respective formulations. Such rapid degradation was to be expected. See EP 0247983 and EP 244380 which are believed to contain the same disclosure as U.S. Patent Nos. 4,853,230 and 4,786,505 (the Lovgren patents) respectively. As can be seen from Figure 3 of Annex 1, pellets produced according to the present invention, remained stable. See Paragraph 15.

It is submitted that taken alone or in their entirety, the declarations establish the non-obviousness of the now claimed subject matter.

On page 11 of the Official Action, the Examiner criticizes the Molina declaration has not shown that the Depui reference is not enabling. As pointed out above, Depui does not provide details of operation and that is why applicant compared to EP '797. *In re Fouche, supra.*

With respect to the Johansson declaration, the Examiner states that because Johansson compared example 5 of Depui '771 rather than Depui '184 that this is a reason not to credit the showing. The Examiner maintains that a showing that Depui '771 is not enabling does not extend to the instant rejection. However, the disclosures of both of the Depui references are extremely close and, as repeatedly pointed out, example 4 of Depui '184 does not provide operational detail for any of the apparatus used in that example. Again, see *In re Fouche*, 169 USPQ 429 at 432 to 433. The main difference between the Depui references is that Depui '771 is directed to a dosage form of a proton pump inhibitor and a prokinetic agent whereas Depui '184 is directed to a dosage form for a proton pump inhibitor and an NSAID. Based on the written disclosures of each of these respective references, and their lack of detail with respect to conditions of process operation, there is

no reason from the prior art to expect a different result if example 4 were produced but without a separating layer. Further, the reason the declarant in the Johansson declaration indicated that the degradation of the prior art composition without a separating layer was not a surprise is because the prior art foretold that degradation would result. See Lovgren '505 or Lovgren '230.

It is not understood how the Examiner can state on page 12 that the instant invention is directed to the same dosage form as disclosed by Depui since Depui is attempting to produce a multiple active ingredient dosage form. In the Examiner's mistaken position, the present claim does not exclude applying a separating layer is also not understood. Clearly, the rejection is not based on the claim language in view of the prior art but is founded on an improper interpretation or application of the term "comprising".

Inherency

Inherency can only be invoked when an event or condition must result not when it may result. There is nothing in the record that provides a basis for reliance on inherency to support an obviousness rejection.

On page 13, the Examiner relies on inherency as an argument for responding to the previously submitted statements in the last Amendment. However, it is well established it is improper to rely on inherency in an obviousness rejection. See *In re Spormann and Heinke*, 150 USPQ 449, 452 (CCPA 1966) (... unable to find, however, any indication in the references that such a step would have the effect which applicants sought and found...). Also see *Ex parte Weitzenkorn*, 97 USPQ 76 (POBA 1952). Also, the Johansson declarations shows that inherency cannot be relied upon.

The issue of the substantially nonporous layer has been previously addressed during prosecution. The Examiner's attention is invited to the originally-submitted figures, at least one of which illustrates the substantially nonporous layer.

Self-Contradiction

Applicant is not engaging in self-contradiction. That Office Action assertion suggests a misunderstanding of the prior art problems and unexpectedness of obtaining a stable dosage form for a benzimidazole proton pump inhibitor by means of the present invention and supports Applicant's position that the now claimed subject matter is not obvious

No Additional Proofs are Required

It is respectfully submitted that at this point in the prosecution, the Examiner's call for additional proofs is unwarranted and untimely. Applicant has submitted no less than three declarations addressing different issues raised by the various Examiners over this extended prosecution. The record shows that the submitted proofs have not been properly considered, have been ignored and have been dismissed or not given proper weight for erroneous reasons. Further, where there is no *prima facie* case, there is no need for additional evidence. See *In re Benno, supra.*

Enablement

The comments regarding what must be shown to demonstrate lack of enablement on page 14 are also in error. The question of enablement goes to claimed subject matter. Applicant has not claimed a pellet *per se*. Applicant has claimed a pharmaceutical dosage form. Such a form must have long term stability. The suggestion that the claims should now recite how long the dosage form is stable is improper. Such characteristics are not

properly recited in a claim. See *Preemption Devices Inc. v. Minnesota Mining & Manufacturing Company,* 221 USPQ 841, 844 (Fed. Cir. 1984) (advantages...do not properly belong in claims...).

Discoloration

The Examiner questions the meaning of discoloration in this context. Those in the art who are familiar with the substituted benzimidazole proton pump inhibitor compounds know that discoloration is an indication of the degradation of the active ingredient. Reference again is made to the Lovgren '505 patent. The Examiner hypothesizes that the source of discoloration is from other than degradation. There is no basis for such conjecture. Again, if the Examiner has relevant factual information, compliance with 37 CFR 1.104(d)(2) is requested.

Scope

On page 15, the Examiner raises the issue of the scope. Once again, those familiar with the substituted benzimidazole proton pump inhibitor compounds know that all of the compounds in that group are acid labile and are easily degraded. See the '230 Patent. On page 15, the Examiner repeats that the question that Applicant has repeatedly addressed as to how stability is obtained in the pharmaceutical dosage form of the invention. The Examiner's question is again premised on the erroneous assumption that because the prior art uses similar or even identical materials, the resulting product will have the same properties irrespective of the processing steps. Also see discussion under inherency, *supra.*

Additional Examples

In the paragraph bridging pages 15 and 16, the Examiner suggests that additional examples are needed. However, once again, those who are familiar with substituted benzimidazole proton pump inhibitor compounds know that compounds in this class behave similarly in terms of acid sensitivity as well as the mechanism of action in the body.

Excipients

As to the bolded underlined text on page 15, see above discussion of Lovgren '505 and Tables 1 to 3. Characterizing something as "unclear" with no expressed basis does not require Applicant to submit additional proofs. More than adequate proofs have been made. Also, see *In re Benno, supra*.

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Claims 15-16, 18-25, 30-31, 33-34, 36, 39-46, and 49 have been rejected under 35 USC § 103(a) as unpatentable over Depui '771 in view of Ohno or Wurster. It is submitted that this rejection is improper and should be withdrawn.

With respect to Depui '771, Applicant incorporates the previously submitted comments and arguments regarding this reference. Applicant also incorporates the above comments and arguments with respect to Wurster '241. Applicant also relies on the previously submitted declarations, especially the Johansson declaration which shows that example 5 of Depui does not result in a stable dosage form when made without a separating layer and any suggestion of inherency in the prior art dosage form is unfounded.

The Examiner cites Ohno as teaching a method for providing an enteric coating on solid dosage forms. The objective of the Ohno disclosure is to enteric coat a dosage form with an aqueous solution of a polymeric substance having carboxyl groups as a water soluble salt and contacting the coated dosage form with an inorganic acid to covert the polymer substance into the water insoluble acid form. As explained to the Examiners during the aforementioned interview, the Office Action misstates the disclosure of Ohno. The Examiner cites to col. 3, ll. 24 to 40, as support for her discussion of Ohno and its application as a reference. However, no where in the Ohno reference is there a disclosure that coating apparatus such as pan coaters, drum-type coaters, or Wurster-type fluidized coaters...are equivalent or the same or operate under the same principle. Rather, Ohno discloses that once someone selects a type of coating apparatus, one can use the same conditions of operation for that particular apparatus in applying either an aqueous-based coating material or an organic solvent based coating material. More specifically, Ohno states:

> There is no difference in principle between the conditions with which the solid dosage forms are coated in accordance with the invention and those with which the aforementioned conventional coaters are operated using a coating solution with an organic solvent.

Thus, the very basis on which the Examiner relies for the citation or combination of Ohno in the rejection is in error. Ohno does not provide a broad teaching of equivalency or suggest that the results obtained by all coating apparatus are equivalent. The Examiner is not free to modify the disclosure so as to suggest that which the actual text does not, *In re Hummer,* 113 USPQ 66, 69 (CCPA 1957). The citation of Ohno highlights that the prior art did not appreciate the significance of the procedure by which the layer is applied. See *Ex parte Wisdom & Hilton*, 184 USPQ 822 (POBA, 1973). The

Examiner suggests that Ohno teaches that all conventional coaters work on the same principle. Assuming that were true, the first Molina declaration shows that you do not obtain satisfactory results from all coaters.

Starting on page 18 and continuing on to page 26, the Examiner responds to the previously submitted arguments. Most of the points the Examiner makes are duplicative of those addressed above and Applicant repeats those comments.

On page 24, the Examiner repeats her position with Ohno and does not address Applicant's previously submitted comments on that reference and in particular the broad interpretation based on extrapolation the Examiner has given to certain disclosure in that reference, more specifically, at column 3, lines 24 to 40.

On page 25, the Examiner again raises the question regarding the substantially nonporous homogeneous layer, an issue which was addressed early in the prosecution. On page 26, the Examiner repeats the erroneous statement that the present example in Depui's example 5 are similar and are thus the layer must necessarily be nonporous. As discussed above, that is simply not true. It is reliance on inherency in support of an obviousness rejection which is improper.

Further, there is no basis for the Examiner to believe that Depui's formulation is stable. Such information cannot be assumed and if the Examiner has independent knowledge, Applicant again calls upon the Examiner to comply with the requirements of 37 CFR §1.104(d)(2).

Claims 15, 16, 18 to 25, 30, 31, 33, 34, 36, 39 to 46 and 49 have been rejected under 35 USC § 103(a) as unpatentable over WO 96/01624 in view Ohno or Wurster. It is submitted this rejection is improper and should be withdrawn.

Applicant advises that the U.S. counterpart to WO 96/01624 ("WO '624") was brought to the Examiner's attention during the telephone interview in 2006. Example 11 of WO '624 is cited by the Examiner as having a core without a separating layer.

The reference makes no mention of a substantially non-porous homogeneous layer.

Applicant' has submitted the Rule 132 declaration of Molina Millán which reports on a comparative test regarding Example 11. Applicant incorporates its discussion of that declaration as set forth in the Voluntary Submission dated July 7, 2006.

On page 28, the Examiner comments on the Rule 132 declaration but once again does not sufficiently address it. The Examiner fails to consider that the submission not only goes to the question of enablement but also goes to the question of non-obviousness in view of the very art which the Examiner has chosen to rely upon as a primary reference. The Office Action repeats that since the prior art made a pellet that is sufficient to show that the reference is enabling. Once again, the standard for enablement is with respect to the claimed invention. As discussed earlier, it is not necessary that the claims recite how long the dosage form is stable for. The claims indicate it is a pharmaceutical preparation. As such, the pharmaceutical preparation must have sufficient stability to be a product. That is sufficient recitation in the claim language to distinguish over the prior art embodiment that may be stable for at most one hour.

Once again, Applicant repeats that those familiar with the art recognize that the discoloration resulting is an indication of degradation.

With respect to the scope of the showing, Applicant submits that it is more than adequate in this instance. Those in the art recognize that all pyridine substituted

benzimidazoles which are proton pump inhibitors are acid labile and unstable under acidic environmental conditions.

It is clear from the disclosure of the specification that Applicant's stability is not due to the specific components. If the Examiner is indirectly raising a question of enablement with respect to the now claimed subject matter, the Examiner is required to come forth with some reasonable basis for such a position. To date, nothing has been offered in any of the Office Actions which question the enablement of the now claimed subject matter.

Claims 47, 48 and 50 have been rejected under 35 U.SC §103(a) as unpatentable over U.S. Patent No. 6,365,184 to Depui in view of Wurster '241 and in view of U.S. Patent No. 5,232,706 Palomo Coll ("Palomo").

Depui '184 and Wurster '241 have been discussed above and those comments are incorporated by reference in response to this rejection.

Palomo discloses a dosage form for omeprazole which follows the teachings of Lovgren '505 in that the dosage form therein has an intermediate coating between the drug containing region of the dosage form and the outer enteric coating. This reference adds nothing beyond the art already cited and considered. It merely identifies certain additional substances which can be used as basic compounds. However, such compounds were also suggested in Lovgren '505.

Claims 47, 48 and 50 have been rejected under 35 USC §103 as unpatentable over Dupui '771 or WO '624 in view of Ohno or Wurster in view of Palomo further in view of Kim. It is submitted that this rejection is improper and should be withdrawn.

Each of these references have been separately discussed above and those comments are incorporated herewith.

The Kim reference discloses a stabilized composition for omeprazole containing a dosage form in the form of a suppository. Neither Kim nor Palomo remedy the deficiencies of the primary references. However, Kim does confirm that the change of color is an indication of degradation for omeprazole type compounds. See the discussion at Column 1 under Background of the Invention.

It is submitted that there is no motivation established on the record to make the combination of references as has the Examiner in any instance. Clearly, these combinations are the product of hindsight reconstruction which is improper. See *In re Grabiak*, 226 USPQ 870, 872, (Fed. Cir. 1985).

In view of the foregoing, reconsideration and allowance of the application with claims 15, 16, 18 to 25, 30, 31, 33, 34, 36 and 39 to 50 are earnestly solicited.

It is believed that no additional fees or charges are required at this time in connection with the present application. However, if any fees or charges are required at this time, they may be charged to our Patent and Trademark Office Deposit Account No. 03-2412.

Respectfully submitted,

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